

544213
Rec'd PCT/PTO 02 AUG 2005

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



10/544213



(43) International Publication Date
14 October 2004 (14.10.2004)

PCT

(10) International Publication Number
WO 2004/087651 A2

(51) International Patent Classification⁷: C07D

(21) International Application Number:
PCT/US2004/008828

(22) International Filing Date: 23 March 2004 (23.03.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/458,094 27 March 2003 (27.03.2003) US

(71) Applicant (for all designated States except US): MERCK & CO. INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): KARKI, Shyam, B. [NP/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). DESHPANDE, Sameer, R. [IN/US]; 126 East

Lincoln Avenue, Rahway, NJ 07065-0907 (US). THOMPSON, Karen, C. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). PAYNE, Anne, H. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). GANDEK, Thomas, P. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(74) Common Representative: MERCK & CO. INC.; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

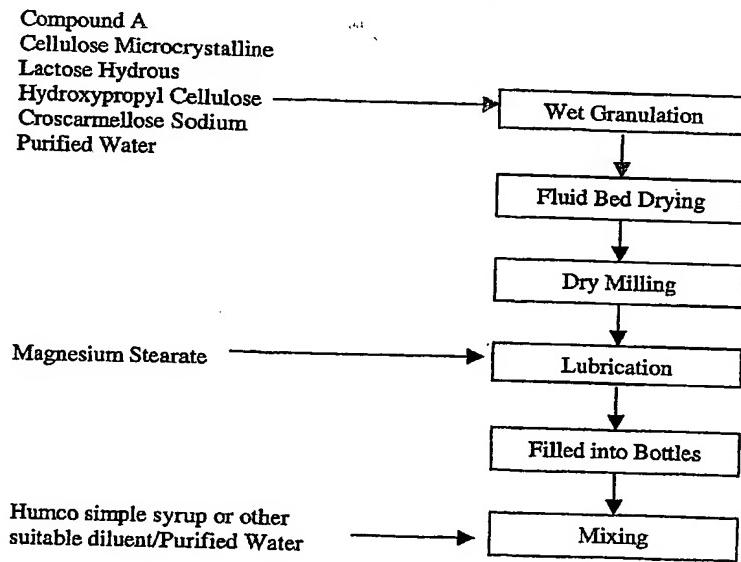
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),

[Continued on next page]

(54) Title: FORMULATIONS FOR TYROSINE KINASE INHIBITORS

Process Flow Diagram for Phase I Manufacturing of a Pediatric Formulations



WO 2004/087651 A2

(57) Abstract: The present invention is related to a powder, powder blend or granulation formulation of 3-[5-(4-methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one, a tyrosine kinase inhibitor, which is adapted for reconstitution with a diluent. This invention is also related to a prepared aqueous suspension, or dispersion, formulation, particularly to a stable oral pharmaceutical formulation, comprising granules of 3-[5-(4-methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one mixed with a diluent. Additionally, the present invention is related to the method of preparing these formulations.